complaining of severe pains in the eye, which exhibited all the symptoms of acute glaucoma. The symptoms, accompanied by severe pain, were much worse upon the following day and continued until the third day, after the onset of the pain, when the eye was enucleated. Section of the eye revealed a small pedunculated tumor about six m. m. in circumference, which was attached to the choroid five or six m. m. from the optic disk. This proved to be a melano-sarcoma.

Examination of the fundus after the onset of pressure symptoms was unsatisfactory on account of cloudiness of the cornea and media of the eye, yet thought I could distinguish, through the retina, vessels of a growth. My principal reliance for the diagnosis was in the glaucomatous symptoms. In a few days after the eye was enucleated, as a safeguard against metastases, the patient was given Coley's fluid hypodermatically daily for one week. The initial dose being one-fourth of a minim and gradually increased to two and three-fourths minims to the dose at the end of the week. The patient now, four years later, is comfortably wearing an artificial eye and has no evidence of an extension of the disease.

Case 2—Mrs. P., age 40, a farmer's wife. Robust health. Came to me on May 5, 1912, for refraction of her left eye, stating that she had lost the sight of her right eye several months before. Examination revealed a large detachment of the retina which was recorded as such and no treatment instituted. More than one year later I was called to her home and found her suffering great pain. Eye hyperaemic with high tension. Unable to see the fundus on account of cloudiness of vitreous. A diagnosis of acute glaucoma was made. Patient being unwilling to go to the hospital for operative treatment, vigorous use of hot stupes, eserine and dionine relieved the pain and hyperaemia in due time, though the cloudiness and some tension remained, when I saw her last, two or three weeks later.

Nothing more was heard from the patient until September of last year, which was four years after I had seen her with the glaucomatous symptoms. She then complained of pain in the blind eye. The globe was hyperaemic, sensitive to touch with some increase of tension. Well up under the upper lid there was a black sacculated protrusion of the sclera. I advised immediate enucleation. This, she refused until one month later. Firm adhesions to thickened tissues of the upper part of the orbit were found. The globe was smoothly enucleated without attempt to remove the adjacent tissue. Complete healing took place in due time and an artificial eye was introduced which the patient has comfortably worn for six months. The larger part of the globe was filled with a black tumorous mass which proved to be melano-sarcoma.

Up to this time no evidence of local or metastatic extension of the disease has occurred. This sad ending will, in all probability, take place sooner or later. In the first case, as the eye was removed very soon after the growth started, and four years having elapsed, we may reasonably hope for no further trouble. Of this, however, we are not certain as recurrence of this character of growth has occurred after the lapse of seven years.[3]

THE PASSAGE OF DRUGS FROM BLOOD SERUM TO THE SPINAL FLUID.*

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In the treatment of diseases of the meninges it is obviously of the greatest importance to be able to cause drugs, and other substances, to pass from the blood stream into the spinal fluid. While the meninges are intact these attempts have met with very small success, except with hexamethylenamin and occasionally with uranin. The possibility of arsenic being able to penetrate seems very doubtful. Sicard and Block, Benedick and others have found traces in the spinal fluid following the intravenous injection of salvarsan, others including the author have been uniformly unsuccessful. This discrepancy may be accounted for by the varying state of meningeal irritation of the syphilitic patients, who furnishes the material for most of these studies.

As early as 1902 Leri as well as Orefici and Cruchet noted the presence of iodide in the spinal fluid of patients suffering with tubercular meningitis who had previously received iodide by mouth. Rotky also was able to detect bromide in the spinal fluid of a patient suffering with meningitis who had received bromide by mouth for a considerable time. None of these authors were able to find either iodide or bromide in the spinal fluid of normal patients. From these observations it would seem that inflammatory disease of the meninges causes a "let down" of the barrier separating blood from spinal fluid, whether at the choroid or elsewhere. Attempts have also been made to reproduce this state by the introduction of irritating substances into the subarachnoid space, such as cyanide of mercury, horse serum and homologous serum. Simple drainage of the spinal fluid following salvarsan, was advocated in America by Pillsbury. Barbat found arsenic in the spinal fluid following a thorough drainage of sub-dural space. In a series of 30 cases treated at Lane Hospital the results of this method (salvarsan following drainage) were definitely inferior to those of the Swift Ellis treatment judged by both subjective symptoms and ability to produce a permanently normal spinal fluid.

All of these observations were more thoroughly explained by the work of Flexner and Amos in their work on poliomyelitis. They showed that anti-bodies and even the virus of the disease might be drawn from the blood serum to the spinal fluid following the introduction of certain irritants into the subarachnoid space. Especially significant was their finding that these irritants might be graded in the order of their potency. Horse serum was found most potent, then heterologous, homologous serum, hypo-tonic and hyper-tonic saline solutions, and least irritating of all was drainage of the cerebrospinal fluid.

It is interesting to consider how these newer

[3] Fox, Practical Treatise of Ophthalmology.

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ideas in spinal pathology have been utilized in our treatments of diseases of the meninges. The intradural methods of Swift Ellis, Ogilvie and Byrnes all tend to place the emphasis upon injecting arsenic or mercury more or less diluted in serum, into the spinal canal. They depend upon diffusion or the circulation of the spinal fluid to bring the injected substance in contact with the pathological lesion. Practically these methods have produced undoubted clinical results, but it well may be that their success may depend on factors other than those given out by their author.

The introduction of the patient's own serum into the subarachnoid space produces an irritation manifested by a pleocytosis frequently as high as 1800 cells per cu. mm. Even drainage of 30 to 50 cc. of spinal fluid may be followed by a mild reaction of 10 to 80 cells. Following the ideas of Flexner and Amos, it seemed possible that this irritation of the choroid would enable drugs and anti-bodies to pass into the spinal fluid for a period of 36 hours.

In order to secure exact information on this point, we attempted to bring sodium iodid from blood to spinal fluid. This drug was chosen for two reasons, first, because it had been definitely proven by numerous observers including Catton that sodium iodid will not penetrate the normal choroid; secondly, because it can be maintained in the blood in considerable concentration with little distress to the patient.

Our technique in brief consisted in injecting 50 grains of sodium iodid in a 10% solution (according to the formula of Klemperer) intravenously every half hour for four injections. One hour after the last injection, 12 cc. of spinal fluid was removed, a cystological examination was made and the fluid was examined for iodine by Mr. C. G. MacArthur of the Pharmacological Department of Stanford University. In these 10 control cases no iodid was found.

In the next group of cases (8) the same routine was followed except that 10 cc. of horse serum was injected into the subarachnoid space six hours before the intravenous injections of iodid. The resulting spinal fluids in six cases showed intense irritation in some cases up to 16,000 cells per cu. mm.—in two cases practically no reaction was obtained. Those cases showing the intense reaction gave definite tests for iodine in the spinal fluid. The two cases showing little or no reaction gave negative tests for iodine.

These results would seem to point to the irritation of the meninges as the essential feature in producing the permeability for iodid.

In another series of cases which will be reported in a subsequent communication, we are attempting to make a quantitative estimation of the arsenic reaching the spinal fluid from the injection of salvarsan where a preliminary injection of horse serum has been given.

These results while of interest from the standpoint of the particular drugs studied are of more importance when viewed in relation to the general methods of intradural medication. If, by these experiments, it seems evident that by an injection of horse serum the night before, sodium iodid may be made to pass from blood to spinal fluid, why should we not use this simple and direct method in our attack on the spirochete located in the meninges? In other words, if horse serum, or preferably the patient's own serum, were given the night before, time allowed for an aseptic reaction to develop, then salvarsan given intravenously, we could obtain the advantage offered by the introduction of the immune bodies present in the patient's own serum and at the same time secure free communication for the penetration of the drug.

We are now treating a series of cases in this fashion in the Neurological Clinic, Stanford University Medical School. It differs from the Swift-Ellis treatment only in reversing the order of the technique—i. e., giving the spinal injection of the patient's own serum, first, with or without the addition of mercury, and following this six hours later by an intravenous injection of salvarsan. While the results seem very encouraging, the series is still too small for an accurate comparison of the merits of this with the older intradural methods.

Discussion.

H. D'Arcy Power: In listening to the papers that have been given and the discussion thereon, I am impressed with the fact that the physiology of these experiments has not been very fully considered. Speaking to one of the writers I gathered from his remarks that in some way or other it was expected that if fluid be withdrawn from the spinal canal a negative pressure would be induced that would cause the absorption of material from the surrounding lymph, by what might be termed a process of mechanical filtration—that is to say, that the meninges would act as a permeable membrane permitting the passage of material like a solution passes through filter paper. It seems to be overlooked that this is not the nature of living tissues, on the contrary these surfaces are covered by an intact physiological membrane made up of separate cells every one of whom is only semi-permeable and not permeable to matter in solution. There is therefore, wherever such surface is intact, a biological selective power which determines whether or not a given salt shall or shall not pass through the membrane. We might very well understand the results obtained by accepting this view, that where fluid does pass in consequence of a disturbance of the intra-meningeal condition such as by the taking out of a large quantity of fluid, or by the introduction of horse serum, or arsenic, that some of the cells lining the meninges, very delicate as they are, suffer such injuries that they undergo necrobiosis, and in every point where a cell so dies, the membrane becomes permeable by removing it from the biological into the physical category. It is only when we properly study the physiology of the passage of solutions through the tissues of the cord that we can expect to make experiments which will have scientific results.

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